REMARKS/ARGUMENTS

Claims 1-5 and 11-13 are pending in this application. Claims 1, 3, 11, and 12 have been amended. No new matter has been inserted. Support for the amendments to claims 1 and 3 can be found throughout the specification and at least at pp. 67 and 105. Applicants request entry of this Amendment and reconsideration of the claims.

35 U.S.C. 112, Second Paragraph

Claims 1-5 and 11-13 are rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner suggests the term "TCCR" is arbitrary and fails to distinctly describe the subject matter of the claims. Applicants respectfully traverse.

While not conceding the correctness of the rejection, in the interest of advancing prosecution, the applicants have amended the claims to define TCCR with reference to specific sequences, (SEQ ID NO: 1 and 2).

Withdrawal of this rejection is respectfully requested.

35 U.S.C. 112, Written Description

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description. In particular, the Examiner asserts the specification does not describe or otherwise reduce to practice a TCCR antagonist. In addition, the Examiner asserts the term "TCCR" is indefinite and thus the structure of a "TCCR" which is antagonized is also not described. Applicants respectfully traverse this rejection.

While not conceding the correctness of the Examiner's position, the applicants have amended claims 1 and 3 to recite the claimed antagonist as an "antibody" or "antibody fragment." As the Examiner has acknowledged that antibodies to TCCR are described in the specification, the amendments to claims 1 and 3 render this written description rejection moot.

Withdrawal of this rejection is respectfully requested.

35 U.S.C. 112, Enablement

Claims 1-5 and 11-13 were rejected under 35 U.S.C. § 112, first paragraph, as not enabled by the specification. The applicants respectfully traverse.

The Examiner contends that the specification does not provide specific guidance to make and use a diverse and representative number of antagonists. While not conceding the correctness of the Examiner's position, the applicants have amended the claims to recite use of anti-TCCR antibodies acknowledged by the Examiner as "not subject to the same uncertainty associated with other molecules." (Office Action, p. 7). Removal of this rejection is requested.

The Examiner further contends that the specification "does not appear to provide a sufficient enabling description of the instant methods of enhancing the differentiation of T-cells into the Th2 subtype, or of treating a Th1-mediated disorder." (Office Action, p. 5). Specifically, the Examiner states that "it is unpredictable as to whether information derived solely from gene inactivation in mice is indicative that the protein inactivated is directly responsible for the observed phenotype." (Office Action, p. 5). The Examiner further states that, "the specification does not appear to provide sufficient objective evidence that a Th1-mediated disease, including inflammatory bowel disease, may be treated by administering any TCCR antagonist in general, or a monoclonal antibody antagonist of TCCR in particular." (Office Action, p. 8). Applicants respectfully traverse this rejection.

Applicants assert that information derived from gene inactivation in mice is highly predictive of efficacy in targeting a gene product for therapeutic intervention, and draw the Examiner's attention to Zambrowicz et al., 2003, *Nat. Rev. Drug Disc.*, 2:38-50. This review article is directed to using mouse knockout models to predict effective treatments based upon the knockout targets. The article states that the current 100 best-selling drugs modulate roughly 43 host targets. Of those 43 host targets, knock out models exist for 34 targets. Of the 34 knockout models:

> "29 of the resulting KO phenotypes have been informative in terms of illuminating gene function and pharmaceutical utility, and providing, in most cases, a direct correlation between KO phenotype and the therapeutic effect of the drug. Overall, concerns about mutations that operate throughout development, gene compensation, embryonic lethality and the differences between mouse and human physiology have not been an issue for the most important targets in the pharmaceutical industry." See p. 40, 2nd col.

Accordingly, applicants assert the Examiner's rejections based upon "unpredictability" of the TCCR gene knockout model are misplaced. As demonstrated in Zambrowicz, the knockout model, in most cases, provides a direct correlation between the knockout phenotype and therapeutic effect.

Further, the specification provides data sufficient to give one skilled in the art a reasonable expectation of success in practicing the claimed methods of treating a Th1-mediated disease with an antagonist of TCCR. In the specification, TCCR deficient cells demonstrated decreased IFN production in response to antigenic stimulation (Figure 16A). TCCR deficient mice exhibited severely reduced titers of ovalbumin specific IgG2a antibodies. (Figure 17B). When TCCR deficient mice were challenged with *L. monocytogenes*, their ability to mount an immune response to the bacteria was impaired. (Figure 17C). These results demonstrate that TCCR deficient mice are impaired in their ability to mount a Th_1 response. (Specification, p. 105).

Therefore, one of skill in the art would have a reasonable expectation of success in treating a Th1-mediated disease in a mammal by administering a therapeutically effective amount of an anti-TCCR antibody or antibody fragment where TCCR has the amino acid sequence of SEQ ID NO: 1 or 2, based on the TCCR -/- mouse model disclosed in the specification.

Withdrawal of this rejection is respectfully requested.

SUMMARY

Applicants submit the claims are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicants' representative to clarify any of the above remarks or to otherwise speed prosecution of this application.

Respectfully submitted,

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